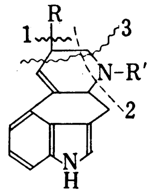

Chart 1

of mode 2 appears markedly. Facility for producting the retro-Diels–Alder reaction seems to be due to substituent at the N^6 position, that is $CONH_2 > H \gg CH_3 > CN$ in order. In case of compounds (V) and (VI), the cleavages of the mode 2 and 3 are not observed but the ion peak at M^+-1 appears remarkably. The characteristic peak induced by 4—5 and 10—11 cleavages is observed.

It is elucidated that the fragmentation of lysergic acid derivatives are drastically influenced by the side chain at the 8 position, the double bond between the 9 and 10 position, and the substituent at the N^6 position.

Experimental

Materials——I was obtained from Sigma Chemical Co. II was extracted from seeds of Morning Glory (Ipomoea Nil Roth),[7] purified by column chromatography[8] and identified with the authentic compound. III was prepared from I by Garbrecht's method,[9] IV, V and VI were supplied by Dr. A. Hofmann, Sandoz Laboratory. VII, VIII, and IX were synthesized from III by the method described in the previous paper.[1]

Mass Spectra——The spectra were measured with a JEOL JMS-01SG double focusing mass spectrometer using a direct insertion probe technique: sample temp., 100—180°; ion-chamber temp., 100—250°; ionizing energy, 75 eV; ionizing current, 200 μA.

Acknowledgement The authors are indebted to Dr. A. Hofmann, Sandoz Laboratory for generously supplying the authentic compounds.

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[7] T. Niwaguchi and T. Inoue, *Eisei Kagaku*, **15**, 290 (1969).

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[9] W.L. Garbrecht, *J. Org. Chem.*, **24**, 368 (1959).

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Effect of Water on Rate of Charge-Transfer Reaction of Aniline with Chloranil[1]

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Charge-transfer (CT) is known to take part in various complexations and reactions. Because the most phenomena of pharmaceutical interest occur in aqueous media, the effect of water on CT has become an important subject in the pharmaceutical field. The previous study[1b] has demonstrated that water promotes the formation of outer complexes. In the present study, attention has been drawn to the rate of CT reaction. As the example in this work, aniline-chloranil system has been taken on which detailed studies carried out with respect to the outer complex formation[3] and the CT reaction.[4]

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[1] *a*) This forms Part X of "Spectroscopic Studies on Molecular Interactions"; *b*) Part IX: I. Moriguchi, S. Fushimi, and N. Kaneniwa, *Chem. Pharm. Bull.* (Tokyo), **20**, 258 (1972); *c*) Presented in part before the 90th Annual Meeting of Pharmaceutical Soceity of Japan, Sapporo, July, 1970.

[2] Location: *Hatanodai, Shinagawa-ku, Tokyo, 142, Japan.*

[3] *a*) P.H. Gore and B.B. Wheals, *Anal. Chim. Acta*, **30**, 34 (1964); D.C. Mukherjee and A.K. Chandra, *J. Phys. Chem.*, **68**, 477 (1964); *b*) I. Moriguchi, S. Fushimi, and N. Kaneniwa *Chem. Pharm Bull.* (Tokyo), **18**, 1553 (1970).

[4] T. Nogami, K. Yoshihara, H. Hosoya, and S. Nagakura, *J. Phys. Chem.*, **73**, 2670 (1969).

Experimental

Materials——Aniline, chloranil, and the solvents used were of analytical grade, and purified by recrystallization or redistillation.

Measurements of Difference Spectra——The difference spectra of mixture of aniline (2×10^{-2}M) with chloranil (1×10^{-3}M) *vs.* chloranil in dioxane containing 0—20% (v/v) water were recorded at regular time intervals at 30° with a Shimadzu model MPS-50L multipurpose spectrophotoneter. The scanning speed was 400 mμ/min. Quatz cells of 1 cm, 0.5 cm, or 0.2 cm path length were used. However, all the absorbance increases were expressed for 1 cm path length in Fig. 1,2, and 3.

Result and Discussion

Aniline and chloranil form an outer complex (1:1) in non-polar sovents,[3a] and also in non-aqueous polar solvents at relatively low concentrations[3b] or at low temperature.[4] In the presence of water, however, the solution becomes brown, and then a reaction product is precipitated.

Fig. 1 shows the spectral change of aniline–chloranil mixture in dioxane containing 0—20 % (v/v) water at about 8 min after preparing the solutions. A strong absorption band appears at 392 mμ and a weak one at 548 mμ. The new bands are probably due to 3,6-dianilino-2,5-dichloro-*p*-benzoquinone (DDB)[5] produced as a result of CT reaction of aniline with chloranil.[4] The intensities of the bands increase with increasing water content of the solvent. However, although chloranil is known to be a good π-electron acceptor stable in various non-aqueous solvents,[6] its dioxane solution gradually turned purple upon the addition of more than 20% (v/v) of water. In the case of many other water-miscible solvents such as alcohols, ketones, and glycols, the smaller amount of water caused a similar color change of chloranil solutions. The coloration seems to be ascribable to the formation of chloranil anion radical as a result of strong CT concerned with solvents. From this reason, dioxane containing 0—20% (v/v) water was used as the solvent throughout the investigation.

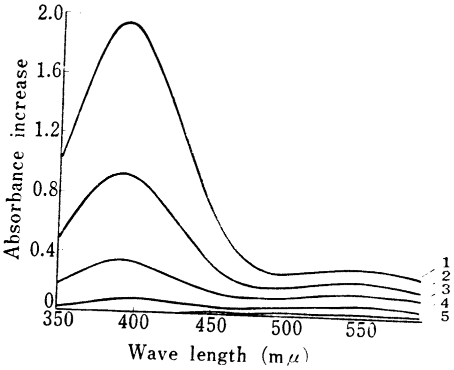

Fig. 1. Differnce Spectra of Aniline-Chloranil System *vs.* Chloranil in Aqueous Dioxane at 30°

2×10^{-2}M aniline plus 1×10^{-3}M chloranil at about 8 min after preparing the test sloutions.
spectra 1—5: in dioxane containing 20, 15, 10, 5, and 0 % (v/v) water, respectively

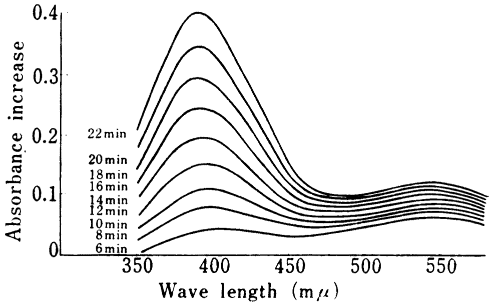

Fig. 2. Absorption Increase of Aniline-Chloranil System in 95% (v/v) Dioxane at 30°

recorded at 6—22 min (at 350 mμ) after preparing the solution of 2×10^{-2}M aniline plus 1×10^{-3}M chloranil *vs.* chloranil with a scanning speed of 400 mμ/min

Fig. 2 shows the time dependence of difference spectra of aniline-chloranil system in 95% (v/v) dioxane. It is seen that the intensity of about 550 mμ region increases immediate-

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5) Visible absorption spectra of DDB: 548 mμ (weak) and 391 mμ (strong) in 2-mthoxyethanol; K. Wallenfels and W. Draber, *Tetrahedron*, **20**, 1889 (1964).

6) I. Moriguchi, S. Fushimi, and N. Kaneniwa, *Chem. Pharm. Bull.* (Tokyo), **19**, 2132 (1971)

ly to some extent and then slowly, whereas the 392 mμ band develops steady and rather rapidly. The initial increase in the 550 mμ absorption may be due to the formation of outer complex or inner complex of aniline with chloranil. On the other hand, the steady increase at 392 mμ seems to be mainly ascribable to the production of DDB. Accordingly, the time dependence of the increase in the 392 mμ absorption was measured at 30°. The result is shown in Fig. 3. A marked increase in absorption is seen for the solution of higher water content. This result may lead to the conclusion that water promotes the CT reaction of aniline with chloranil.

According to the stoichiometry proposed by Nagakura and his co-workers,[4] the CT reaction of aniline (A) with chloranil (C) is expressed as

$$\mathrm{A} + \mathrm{C} \underset{k_2}{\overset{k_1}{\rightleftarrows}} \text{outer complex} \xrightarrow{k_3} \text{inner complex} \underset{+\mathrm{A}}{\xrightarrow{k_4}} \mathrm{DDB} \tag{1}$$

The rates of association and dissociation of the outer complex may be much faster than the rate of its conversion into the reaction product through the inner complex, *i.e.*, k_1, $k_2 \gg k_3$, k_4. Such being the case, the rate equations of the reaction under the experimental condition where the concentration of aniline is much higher than that of chloranil[7] are

$$-\frac{d(c-x)}{dt} \doteqdot k_3 a(c-x) \tag{2}$$

$$\frac{d(x-y)}{dt} \doteqdot k_3 a(c-x) - k_4 a(x-y) \tag{3}$$

where a and c are the initial concentrations of aniline and chloranil, respectively, x is the total concentration of inner complex plus DDB, and y the concentration of DDB. On integration, Eq. (2) gives

$$c - x \doteqdot c e^{-k_3 a t} \tag{4}$$

On substitution of Eq. (4) into Eq. (3) and integration, we obtain

$$x - y \doteqdot \frac{c k_3}{k_3 - k_4}\left(e^{-k_4 a t} - e^{-k_3 a t}\right) \tag{5}$$

From Eq. (4) and (5), y is given by

$$y \doteqdot c\left(1 + \frac{k_4}{k_3 - k_4} e^{-k_3 a t} - \frac{k_3}{k_3 - k_4} e^{-k_4 a t}\right) \tag{6}$$

On the assumption that $k_4 = m k_3$ for the convenience of numerical analysis, Eq. (6) now becomes

$$y \doteqdot c\left(1 + \frac{m}{1-m} e^{-k_3 a t} - \frac{1}{1-m} e^{-m k_3 a t}\right) \tag{7}$$

It may be assumed that 392 mμ absorptions of the component molecules and their outer and inner complexes can be neglected as compared with the strong band of DDB. Then, the values of k_3 and k_4 were so estimated that the experimental data of absorption increase at 392 mμ might best fit to Eq. (7).

The values of k_3 and k_4 thus estimated are listed in Table I. The cruves, calculated by using Eq. (7) with the k_3 and k_4 values in Table I, of the 392 mμ absorption increase against time are drawn in Fig. 3. The agreement of the calculated curves with the observed values

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[7] The initial concentration of aniline was 20 times as high as that of chloranil throughout our experiments.

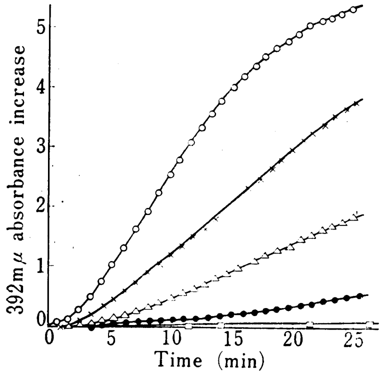

Fig. 3. Time Dependence of Absorption Increase for Aniline-Chloranil *vs.* Chloranil in Aqueous Dioxane at 392 mμ and 30°

solvents: dioxane containing 20 (○), 15 (×), 10 (△), 5 (●), and 0 (□) % (v/v) water

———: calculated curves by using Eq. (7) with the values of k_3 and k_4 in Table I, m being 1.5, and increase in molar absorptivity by the conversion into DDB being 6.15×10^3

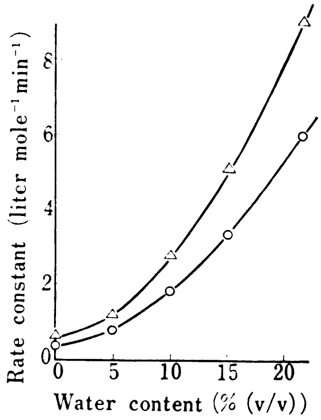

Fig. 4. Plots of Rate Constants, k_3 and k_4, *vs.* Water Content of the Solvents

—○—: k_3, —△—: k_4

TABLE I. Rate Constants for CT Reaction of Aniline with Chloranil in Aqueous Dioxane at 30°

Water content (% (v/v))	k_3 (liter/mole min)	k_4 (liter/mole min)
0	0.19	0.29
5	0.77	1.16
10	1.85	2.78
15	3.36	5.04
20	6.00	9.00

seems satisfactory. As is clearly seen in Fig. 4, both k_3 and k_4 markedly increase with increasing water content of the solvent.

Thus, it may be concluded that water promotes the formations of inner complex and CT reaction product in the case of aniline-chloranil mixture which is one of the most typical donor-acceptor systems.

The promoting effect on the CT reaction seems to be ascribable to the enhancement of polarity of the media by water. However, the detailed mechanism is uncertain.